UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,750	09/30/2003	Vitaly J. Vodyanoy	035721/267665	4229

826 7590 08/10/2004

ALSTON & BIRD LLP
BANK OF AMERICA PLAZA
101 SOUTH TRYON STREET, SUITE 4000
CHARLOTTE, NC 28280-4000

EXAMINER	
MONDESI, ROBERT B	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/674,750	VODYANOY ET AL.	
	Examiner	Art Unit	
	Robert B Mondesi	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *October 30, 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Priority

The current application filed on September 30, 2003 claims priority to provisional application 60/415,108 filed on September 30, 2002.

Information Disclosure Statement

The IDS filed February 19, 2004 has been received and is signed and considered, a copy of PTO-1449 is attached to the following document.

Specification

The disclosure is objected to because of the following informalities:

The use of the trademarks MILLIPORE (Page 16, Line 3), BIO-RAD, SIGMA (Page 19, Line 3), DNEASY TISSUE KIT (Page 20, Line 20), QUANTINATION REAGENT (Page 20, Line 19), OLYMPUS (Page 22, Line 1), CCD VIDEO CAMERA SYSTEM (Page 22, Line 4), PIERCE SLIDE-A-LAZER 10K (Page 22, line 20), READY GEL (Page 23, Line 3), ATCC (PAGE 26, Line 18) SIGMA, HYCLONE (Page 26, LINE 19), BIORAD (Page 27, Line 9) and ELISA (Page 32, Line 19) have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode co0ntemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 and 5-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of cyclic amplification of proteons, in a plasma sample, comprising six cycles of incubation for 15 minutes at 60° C, does not reasonably provide enablement for a method of cyclic amplification of proteons in a biological sample involving steps 1a), 1b), 1c), 2a), 2b), 2c), and 2d). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use and make the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir.1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single,

simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the relative skill of those in the art, (5) the predictability or unpredictability of the art, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that

experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1.Breadth of the claims.

In regards to the method of the invention and the breadth of the claims the broadest interpretation that applies is a method of cyclic amplification of proteons in a biological sample involving steps 1a), 1b), 1c), 2a), 2b), 2c), and 2d).

2. The nature of the invention.

The invention is designed to provide a method of amplifying/increasing the amount of misfolded protein aggregates, known as proteons, in a biological sample. Applicants method involves using heat and centrifugation to accomplish the method of their invention.

3. The state of prior art.

In regards to the method of the invention, cyclic amplification of proteons, the prior art teaches a method of amplification using cycles of sonication, not heat, to increase the amount of proteons (Soto et al.). Soto et al. teach that specific treatments of a sample containing the prion prominent glyco-protein PrP^{C} with cycles of sonication will lead to a conformational change of PrP^{C} to PrP^{Sc} and hence increases the amount of proteons in a plasma sample. The prior art does not discuss the cyclic amplification of proteons using heat treatment.

4. The relative skill in the art.

The relative skill in the art as it relates to the administering of therapeutic polypeptides used for the treatment, inhibition, prevention or amelioration of pancreatic disorder is characterized by that of a M.D. or Ph. D. level individual.

5. The level of predictability in the art.

The level of predictability of cyclic amplification of proteons in the art is low since there is not much known about cyclic amplification of proteons using any other method than the method of Soto et al. which uses intervals of sonication and, also since, the prior art does not suggest that random treatments of biological samples with heat and centrifugation for an undetermined amount of time will lead to an increase in the amount of proteons in a sample.

6. The amount of guidance present.

All the guidance present is in view of a method of cyclic amplification of proteons in a plasma sample comprising six cycles of incubation for 15 minutes at 60° C. The applicants have not provided guidance or shown to a person skill in the art how a method of cyclic amplification of proteons involving random treatments of a biological sample with heat and centrifugation will lead to an increase of the amount of proteons in the mentioned sample.

7. The existence of working examples.

The specification on page 32 (Example 8) and Figure 2 provides working examples of a method of cyclic amplification of proteons in a plasma sample comprising of six cycles of incubation for 15 minutes at 60° C, but no examples pertaining to alternative number of cycles or temperature ranges have been disclosed.

8. The quantity of experimentation necessary.

In the case of a method of cyclic amplification of proteons in a biological sample involving steps 1a), 1b), 1c), 2a), 2b), 2c), and 2d) a large quantity of experimentation would be required to practice the invention since the specification has not shown to a person skill in the art how random treatments of biological samples with heat and centrifugation for undetermined amount of time will lead to an increase in the amount of proteons in a plasma sample.

Due to the large quantity of experimentation necessary to provide evidence that the claimed method of invention will increase the amount of proteons, the lack of guidance presented in the specification regarding the same, the absence of a working example directed to same, the unpredictable nature of the invention with regards to cyclic amplification of proteons using heat, the state of the prior art not providing any evidence for any methods of cyclic amplification of proteons in a biological sample using random cycles of heating and centrifugation, and the breath of the claims which fails to provide particular steps involved in cyclic amplification of proteons in a biological sample using heat and centrifugation, the specification fails to teach the skilled artisan in the art how to make and use the invention.

Claims **1-3 and 5-14** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In **claims 1-2** the phrase "a period of time" has not been defined in the claims or in the specification of the present application.

In **claim 3** the phrase "predetermined number of cycles" has not been defined in the claim or the specification of the present application.

Claim 4 recites the limitation "the proteons produced" in line 11. There is insufficient antecedent basis for this limitation in the claim.

In **claim 4** line 1 the applicants make reference to disorders in tables 1 and 2, in situations wherein the applicant can define the limitations of a claim in words it is not permitted to make references to a table (MPEP 2173.05). Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." Ex parte Fressola, 27USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 15-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Bush et al. (cited in the IDS filed February 14, 2004). **Claims 17-18** are product by process claims and even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-

process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Bush et al. disclose an isolated proteon nucleation center comprising a Zinc metal cluster (pages 1464-1467) (**present claim 15 and 17-18**). In **claim 16**, the applicant cites a purification method involving the separation of misfolded protein aggregates using ultrafiltration membranes (Millipore, Centricon 5000 daltons). Bush et al. teach in their publication that misfolded protein aggregates can be isolated from plasma samples using microfilteration or ultrafilteration membranes (Pages 1464-1467). Thus Bush et al. teach all the elements of **claims 15, 17-18** and these claims are anticipated under 35 USC 102(b).

Claims 15 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Campbell et al. (cited in the IDS filed February 14, 2004). Campbell et al disclose a proteon nucleation center that can be used to promote cell death in cell culture (Prion Protein, Page 127, Column 1, lines 19-22) (**present claim 15 and 19**). Thus Campbell et al. teach all the elements of **claims 15, 19** and these claims are anticipated under 35 USC 102(b).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert B Mondesi
Patent Examiner
Group 1653
08-03-04

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER